Long-term Outcomes of Stereotactic Radiosurgery for Skull Base Tumors Involving the Cavernous Sinus

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Research Article

Keywords: cavernous sinus, skull base tumors, stereotactic radiosurgery, gamma knife radiosurgery

Posted Date: October 20th, 2021

DOI: <https://doi.org/10.21203/rs.3.rs-986293/v1>

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Version of Record: A version of this preprint was published at Journal of Neuro-Oncology on January 14th, 2022. See the published version at <https://doi.org/10.1007/s11060-021-03921-5>.

Abstract

Purpose

Stereotactic radiosurgery (SRS) is an effective and less invasive therapeutic option for cavernous sinus (CS) tumors. However, its long-term effectiveness and neurological outcomes have yet to be fully elucidated. We aimed to examine the long-term outcomes of SRS for CS tumors.

Methods

Overall, 127 patients with benign CS tumors, including 91 with meningioma, 14 with trigeminal schwannoma (TS), 14 with non-functioning pituitary adenoma (PA), and eight with cavernous hemangioma (CH), treated with SRS at our institution from 1990 to 2018, were included. Tumor control and functional preservation/recovery were evaluated in detail.

Results

The mean post-SRS follow-up period was 102 months. The progression-free survivals (PFSs) were 97% at 5 years, 90% at 10 years, and 88% at 15 years for the entire cohort; 96% at 5 years and 87% at 10 years for meningiomas; and 100% at 10 years for the other tumors. No significant difference was observed among the tumor types (log-rank test; meningioma vs. TS, $p = 0.232$, meningioma vs. PA, $p = 0.297$, meningioma vs. CH, $p = 0.277$). Improvement in cranial nerve (CN) function was observed in 35 (27%) patients. TSs tended to show CN improvements more often than meningiomas did (total improvements, 62% vs. 23%; $p = 0.004$, eye movement function, 100% vs. 20%; $p = 0.002$). Deterioration, or development of new CN deficits, was observed in 11 (9%) patients.

Conclusion

SRS provides durable tumor control and contributes to sufficient preservation of CN function.

Introduction

The cavernous sinus (CS) is an important anatomical structure containing the internal carotid artery (ICA), and the third, fourth, fifth, and sixth cranial nerves (CNs). A variety of benign tumors, such as meningiomas, trigeminal schwannomas (TS), pituitary adenomas (PA), and cavernous hemangiomas (CH), can arise in or extend into this structure, causing impairment of visual function, extraocular movement, facial sensory function, and other CN functions [1–4]. Surgical resection is the standard primary treatment to achieve immediate mass reduction and obtain a histopathological diagnosis. Despite well-established microscopic and endoscopic skull base techniques, surgical interventions for such tumors remain challenging due to their deep skull base location and proximity to the ICA, CNs, visual pathways, and pituitary gland. Preservation of CN may require surgeons to leave tumor remnants behind, and tumor recurrence/regrowth is possible [5–7]. Radiotherapy plays an important role in balancing tumor control and functional preservation, but whether functional recovery is achievable following radiotherapy remains questionable, especially in cases of large symptomatic tumors, since immediate mass reduction is not achievable [6].

Stereotactic radiosurgery (SRS) is a less invasive treatment option utilizing head fixation and highly focused narrow beam radiation that enables precise targeting with a steep dose fall-off. Given the structural features of the CS in which the CNs run along its outer wall, it is theoretically feasible to intensely irradiate tumors while minimizing irradiation to the CNs. Previous literature has reported favorable short- to mid-term outcomes, following either SRS alone or in combination with surgery [8–11]. CS-specific radiation-induced adverse events (RAE), deterioration of CN III–VI function, and ICA stenosis/occlusion, albeit rare, have been reported [12–18]. However, there remains a paucity of data on its long-term outcomes.

This study aimed to clarify the long-term outcomes of tumor control and CN functioning following SRS for benign CS tumors.

Methods

Patient and tumor characteristics

The data of 190 patients with CS tumors, treated with SRS from June 1990 to June 2018 at our institution, were collected from the institutional gamma knife database. Both intra-CS tumors and para-CS tumors extending into the CS were defined as CS tumors. The exclusion criteria were: (1) functioning PAs that required extraordinary high dose irradiation (25 Gy or higher) (n = 22), (2) pathologically confirmed non-benign tumors, including World Health Organization (WHO) grade II/III meningiomas (n = 12), hemangiopericytomas (n = 1), chordomas (n = 18), chondrosarcomas (n = 9), and metastatic tumors (n = 1). As a result, data on 127 patients with benign CS tumors, including 91 meningiomas, 14 TSs, 14 non-functioning PAs, and 8 CHs, were included in the analysis.

Most diagnoses were based on histopathological findings from prior surgery (n = 89). The timing of SRS for postoperative recurrent (n = 45) or residual tumor (n = 44) was determined using the judgment of the surgeon or referring physician or by patient request, without any arbitrary selection. Radiographic diagnosis, without prior surgery, was used in 38 cases (19 meningiomas, 12 TSs, and 7 CHs). All radiographic images were reviewed by two independent neuroradiologists and attending neurosurgeons. The study was approved by the Institutional Review Board of our institution (#2231) and conducted in compliance with the principles of the Declaration of Helsinki and the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines. All patients provided written informed consent for study participation.

The procedures and techniques of SRS

Leksell Gamma Knife (Elekta Instruments, Stockholm, Sweden) was used for all SRS treatments. The detailed treatment process is reported in a previous paper [19, 20]. After head fixation using a Leksell frame (Elekta Instruments, Stockholm, Sweden), stereotactic imaging (CT before July 1996, MRI between August 1996 and January 2018, followed by cone-beam CT) was performed to obtain precise tumor data. Neurosurgeons and radiation oncologists performed radiosurgical planning using commercially available software (KULA planning system) until 1998 and Leksell Gamma Plan thereafter [Elekta Instruments]). In principle, 14–16 Gy was prescribed to the tumor margin using a 50 ± 5 % isodose line. If the tumor was suspected to be aggressive and was sufficiently distant from radiosensitive cerebral structures, such as the optic apparatus or the brainstem, the tumor margin dose was increased to 16 Gy to achieve long-term tumor control.

Follow-up and treatment outcomes

After SRS, MRI was regularly performed every six months for the first couple of years and annually thereafter. Radiographic findings were independently assessed by neuroradiologists and neurosurgeons. Transient expansion, typically occurring in schwannomas due to radiation-induced tumor swelling at around six months after SRS, followed by shrinkage at approximately 18 months, was meticulously distinguished from actual tumor progression by evaluating consecutive MRIs [21, 22]. The neurological status of the patients and their responses to treatment were prospectively collected at each hospital visit, and a Common Terminology Criteria for Adverse Events (CTCAE, version 5.0) grade was retrospectively assigned on the basis of the descriptions. Data on patients who dropped out of regular follow-ups or returned to referring physicians were collected via telephone conversation, and follow-up radiographic images were obtained for our independent review.

Statistical methods

Baseline characteristics of the patients were compared using the chi-square test for categorical variables and the Mann–Whitney U test for continuous variables. Progression-free survival (PFS) rates were calculated using the Kaplan–Meier method and compared among tumor types using the log-rank test. A tumor was considered "progression-free" if there was no > 2-mm increase in tumor diameter in any direction on two or more consecutive post-SRS imaging studies. Factors associated with PFS were examined using bivariate and multivariable Cox proportional hazard analyses. Continuous variables were entered into models after being dichotomized using their median values. Where post-SRS recurrence/regrowth was confirmed, recurrence patterns and features were examined in more detail. Post-SRS CN outcomes were summarized, and factors associated with functional improvement, deterioration, and new deficits were examined with logistic regression analysis, and these rates were calculated and compared using the Kaplan–Meier method. Statistical analyses were performed using JMP Pro 15 software (SAS Institute Inc., Cary, NC, USA).

Results

Participant characteristics

Patient characteristics are shown in Table 1. The mean post-SRS follow-up period was 102 months ($\pm$ standard deviation [SD] of 79 months). When comparing the baseline characteristics between tumor types, the maximum diameter (30 mm vs. 24 mm; $p = 0.029$) was significantly larger, and the prescription dose (15.9 vs. 14.6 Gy; $p = 0.012$) and central dose (33.4 vs. 30.7 Gy; $p = 0.039$) were significantly higher in meningiomas than in TS. Patients underwent prior surgery significantly more often in the meningioma group than the TS and CH groups (meningioma 79%, TS 14% [$p = 0.001$], and CH 13% [$p = 0.001$]). Of those, 21 patients with meningioma (23%), and three patients with PA (21%) had had surgery two or more times before SRS.

Table 1
Baseline characteristics of the patients

Variables	All tumors (n = 127)	Meningioma (n = 91)	Trigeminal schwannoma (n = 14)	Non-functioning pituitary adenoma (n = 14)	Cavernous hemangioma (n = 8)	p-value		
						TS ^a	PA ^a	CH ^a
Mean ± SD						Mann–Whitney U test		
Age, years	54 ± 12	55 ± 11	50 ± 16	55 ± 12	58 ± 11	0.128	0.731	0.339
Follow-up, months	102 ± 79	108 ± 79	87 ± 87	73 ± 69	121 ± 86	0.176	0.065	0.504
Maximum diameter, mm	28.7 ± 9.1	30.0 ± 10.1	24.0 ± 4.4	26.9 ± 8.4	25.6 ± 3.5	0.029*	0.320	0.266
Target volume, cm ³	7.1 ± 6.8	8.1 ± 7.6	4.3 ± 2.5	5.1 ± 3.7	5.4 ± 2.2	0.063	0.262	0.676
Prescription dose, Gy	15.6 ± 1.9	15.9 ± 2.0	14.6 ± 1.4	15.4 ± 0.8	14.8 ± 1.4	0.012*	0.404	0.149
Central dose, Gy	32.9 ± 5.5	33.4 ± 5.8	30.7 ± 5.0	32.9 ± 4.2	31.3 ± 3.9	0.039*	0.989	0.199
n [%]						chi-square test		
Males	32 [25]	20 [22]	4 [29]	6 [43]	2 [25]	0.584	0.092	0.844
Prior surgery	89 [70]	72 [79]	2 [14]	14 [100]	1 [13]	0.001*	0.059	0.001*
GTR at the latest surgery	7 [8]	6 [8]	0	1 [7]	0	0.064	0.098	0.150
STR at the latest surgery	77 [87]	61 [85]	2 [100]	13 [93]	1[100]	0.001*	0.049	0.001*
* Significant at $p < 0.05$.								
^a Reference: meningioma								
GTR, gross total resection; SD, standard deviation; STR, subtotal resection								

Tumor control

Of all the patients, 126 (99%) were alive at the final follow-up visit, and the single death was due to suicide, unrelated to the tumor and associated treatment. At the last follow-up, 56 (44%) tumors had decreased in size, 61 (48%) remained unchanged, and 10 (8%) increased in size. Tumor shrinkage was observed in 32 patients (35%) with meningioma, 10 (71%) with TS, seven (50%) with PA, and seven (81%) with CH. Tumor progression was not observed except for ten patients with meningioma. In the entire cohort, the PFS was 97% at 5 years, 90% at 10 years, and 88% at 15 years (Figure 1A). The tumor specific PFS was 96% at 5 years, 87% at 10 years for meningioma, and 100% at 10 years for the other tumors. There were no significant differences among tumor types in PFS ((log-rank test; meningioma vs. TS, $p = 0.232$; meningioma vs. PA, $p = 0.297$; meningioma vs. CH, $p = 0.277$; Figure 1B). PFS was 100% at 5 years and 94% at 10 years with SRS alone; 96% at 5 years and 89% at 10 years for SRS with prior surgery (log-rank test; $p = 0.082$, Figure 1C).

Since tumor recurrence was observed only in meningiomas, the analysis of potential risk factors for tumor recurrence were performed in meningiomas. No significant factors were found in the bivariate and multivariable analyses (Online Resource Supplementary Table 1). Patients with post-SRS recurrence are summarized in Online Resource Supplementary Table 2. All recurrences occurred in meningiomas, a median of 87 months (range, 14-208 months) after SRS. Nine (90%) tumors were post-surgical recurrence, and three (30%) tumors were treated with suboptimal radiation coverage because of proximity to the optic apparatus or brainstem structure. The patterns of recurrence were intra-field in four (40%) patients and marginal (recurrence occurred out of the radiation field but within 20% isodose line) in six (60%). PFS in meningioma was 100% at 5 years and 89% at 10 years for SRS alone; 95% at 5 years and 87% at 10 years for SRS with prior surgery (log-rank test; $p = 0.207$, Figure 1D).

Improvement of cranial nerve deficits

The details of CN function are summarized in Table 2. Eighty-seven patients (69%) had 132 CN deficits before SRS. The rate of pre-SRS CN deficits was the highest in meningiomas (69/91, 76%), followed by 12 (86%) in TSs, four (29%) in PAs, and two (25%) in CHs.

Table 2
Improvement and deterioration of cranial nerve function after radiosurgery, stratified by tumor type

Improvement in cranial nerve function								
Variables	All tumors (n = 87)	Meningioma (n = 69)	Trigeminal schwannoma (n = 12)	Non-functioning pituitary adenoma (n = 4)	Cavernous hemangioma (n = 2)	p-value		
						TS ^a	PA ^a	CH ^a
Pre-SRS total deficits, (n)	132	111	13	4	4			
II, n (%)	4 (16)	4 (20)	/ [†]	0 (0)	0 (0)	N/A	0.394	0.484
EOM (III, IV, VI), n (%)	11 (24)	8 (20)	3 (100)	0 (0)	0 (0)	0.002*	0.624	0.624
V, n (%)	16 (36)	11 (31)	5 (50)	/ [†]	/ [†]	0.279	N/A	N/A
Ptosis, n (%)	1 (50)	0 (0)	/ [†]	/ [†]	1 (100)	N/A	N/A	0.157
VII, n (%)	2 (33)	2 (33)	/ [†]	/ [†]	/ [†]	N/A	N/A	N/A
VIII, n (%)	1 (17)	1 (17)	/ [†]	/ [†]	/ [†]	N/A	N/A	N/A
IX, X, n (%)	0 (0)	0 (0)	/ [†]	/ [†]	/ [†]	N/A	N/A	N/A
Total improvements, n (%)	35 (27)	26 (23)	8 (62)	0 (0)	1 (25)	0.004*	0.271	0.942
Deterioration of cranial nerve function								
Variables	All tumors (n = 127)	Meningioma (n = 91)	Trigeminal schwannoma (n = 14)	Non-functioning pituitary adenoma (n = 14)	Cavernous hemangioma (n = 8)	p-value		
						TS ^a	PA ^a	CH ^a
II, n (%)	1 (1)	1 (1)	0 (0)	0 (0)	0 (0)	0.694	0.694	0.766
EOM (III, IV, VI), n (%)	4 (3)	4 (4)	0 (0)	0 (0)	0 (0)	0.424	0.424	0.545
V, n (%)	6 (5)	5 (5)	1 (7)	0 (0)	0 (0)	0.805	0.369	0.496

Overall post-SRS improvement of any CN function was observed in 27 of 87 patients (31%).

* Significant at $p < 0.05$

[†] no symptomatic patients in this group

^a vs. meningioma

CH, cavernous hemangioma; CN, cranial nerve; EOM, extraocular movement; PA, non-functioning pituitary adenoma; SRS, stereotactic radiosurgery; TS, trigeminal schwannoma

N/A, no improvement in the relevant cranial nerve function.

Improvement in cranial nerve function								
Others (ptosis, VII, VIII, IX, X), n (%)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	N/A	N/A	N/A
CTCAE grade ≥ 3 , n (%)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	N/A	N/A	N/A
Total deficits	11 (9)	10 (11)	1 (7)	0 (0)	0 (0)	0.662	0.192	0.323
Overall post-SRS improvement of any CN function was observed in 27 of 87 patients (31%).								
* Significant at $p < 0.05$								
† no symptomatic patients in this group								
^a vs. meningioma								
CH, cavernous hemangioma; CN, cranial nerve; EOM, extraocular movement; PA, non-functioning pituitary adenoma; SRS, stereotactic radiosurgery; TS, trigeminal schwannoma								
N/A, no improvement in the relevant cranial nerve function.								

In the entire cohort, CN improvement was observed in 35 (27%) deficits, including four (16%) visual deficits, 11 (24%) third, fourth, and sixth CN deficits, 16 (36%) trigeminal neuropathy and one (50%) ptosis. Among tumor types, improvement of third, fourth, and sixth CN deficits was significantly more common in patients with TS (100%) than in meningioma (20%, $p = 0.002$), whereas no significant difference was observed in improvements in the other CN deficits. The cumulative rates of post-SRS improvement of CN functions are shown in Figure 2A. The post-SRS CN improvement was observed at a mean $\pm$ SD of 17 ± 14 months. More significant improvements were observed in TSs than in meningiomas (log-rank test; $p = 0.001$, Figure 2B). The improvement rates of CN V (57% vs. 26%; $p = 0.025$) and all CN (41% vs. 21%; $p = 0.025$) were significantly higher in SRS alone than in SRS with prior surgery (Online Resource Supplementary Table 3). Additionally, 105 CN deficits caused by tumor compression were relieved in 32 patients (30%) after SRS.

Radiation-induced adverse events

Details of new or worsened CN deficits following SRS are shown in Table 2. Eleven (9%) CN deficits had deteriorated or newly developed at a mean period of 19 ± 28 months following SRS, including one (1%) visual deficit, four (3%) extraocular movement disorders, and six (5%) trigeminal neuropathies. All were mild or transient (CTCAE grade 1–2). The cumulative rates of post-SRS deteriorated/newly developed CN functions are shown in Figure 2C. There were no significant differences among tumor types (Figure 2D). Aside from the CN deficits, hydrocephalus was observed in one patient (0.8%) with well-controlled meningioma who underwent ventriculoperitoneal shunting 100 months after SRS. In this case, the association between the tumor and hydrocephalus was unclear. No temporal lobe necrosis was observed in the entire cohort. Post-SRS signal change, as a high-intensity signal change on T2-weighted imaging in the temporal lobe, was identified in two patients with meningioma (1.6%) 3–6 months after SRS; both were asymptomatic and diminished at 13–24 months. Hypopituitarism was observed in one patient (0.8%) with meningioma 47 months after SRS, and asymptomatic ICA stenosis was observed in one patient (0.8%) with meningioma 169 months after SRS.

Discussion

In this study, we analyzed long-term outcomes of SRS for CS tumors. Using a similar radiosurgical strategy, we defined the tumor margins and prescribed conformally and selectively a marginal dose of 14–16 Gy; the 10-year PFS was 90%, with the post-SRS CN improvement rate reaching 27%, while maintaining a low CN deterioration rate (9%). These results

suggest that SRS would be a reasonable treatment option, providing long-term tumor control with favorable neurological outcomes.

The results showed that the tumor control rate is excellent, especially in non-meningioma CS tumors. Most baseline characteristics of tumors in this cohort were similar, with differences in tumor size and the history of prior surgery. The differences in PFSs between meningioma and non-meningioma tumors possibly reflected differences in tumor biology, which might be due to selection bias in that most meningiomas are postoperative cases. In the literature, tumor control rates were reported to be 77–100% in TS at median observation periods of 27–91 months, 89–100% in non-functioning PA at 36–67 months, and 100% in CH at 30–40 months [13–18, 23–28]. Our data are comparable to these studies.

The post-SRS CN improvements were also excellent, likely the result of the high tumor shrinkage rate. Regarding RAEs, our study demonstrated excellent functional preservation rates, which might be due to the highly selective high dose irradiation which SRS can provide. Therefore, non-meningioma CS tumors are an excellent indication for SRS.

Treatment strategies need to be formulated according to the characteristics of individual tumors. PA tumors often have a preexisting effect on the optic nerve, and surgical decompression should often be prioritized. SRS plays an adjunctive role for recurrent/residual tumors and can be a primary treatment modality in TS and CH.

The PFS of meningioma was slightly lower than that of non-meningiomas but was still satisfactory at 96% at 5 years and 87% at 10 years. Most previous retrospective studies and the International Stereotactic Radiosurgery Society Practice Guidelines reported excellent tumor control rates of 86–99% at 5 years and 69–97% at 10 years with favorable functional preservation rates of 80–100%, consistent with our results [19, 29–40]. We found that six (60%) recurrent meningiomas presented with marginal recurrences after a mid-to-long period of tumor control (range, 67–208 months). Recurrences can be explained by the intrinsic features of meningiomas. They easily blend in the meninges, making it challenging to accurately define tumor margins. It is important to meticulously pursue dural tails using thin-slice MRIs. In post-surgical recurrence/regrowth cases, surgical scar tissue might obscure the true tumor margins. Nine (90%) recurrences were postoperative cases, and in situ comparisons to pre-operative images may highlight the true extent of the tumor. Although the role of surgery remains debatable, and immediate mass reduction may be necessary in certain cases, primary SRS may be reasonable for selective cases with small- to medium-sized CS tumors, unless the tumor has atypical radiographic features. Four (40%) cases had in-field recurrence, and three were likely explained by suboptimal coverage because of the proximity of the optic chiasm and brainstem or incomplete coverage of a tumor part extending into the tentorial edge. The remaining case had a WHO grade I tumor with biologically aggressive features, including a Ki-67 index of 15%.

CN dysfunction as post-SRS RAEs has occurred in 1–23% of patients in the past [8–10, 14–19, 23, 24, 26, 27, 30–34, 37–42]. In our study, 11 of all 127 patients (9%) experienced deterioration or emergence of new CN dysfunction after SRS, which was lower than previously reported (Online Resource Supplementary Table 4). Notably, 10 of 11 (91%) of these occurred in patients with CS-meningioma. There was no significant difference among tumor types, and all of the dysfunctions were either CTCAE grade 1 or 2. Comparing surgery and SRS, a meta-analysis of 2065 CS-meningiomas showed that the incidence of neurological complications was significantly lower with SRS alone (25.7%) compared with SRS after surgery (59.6%) [43]. We failed to find a similar pattern, which could be explained by our relatively small patient number, although it might be due to our lower RAE rate. A certain portion of RAEs may be avoidable by meticulously defining tumor margins and reducing direct irradiation to the CNs using thin-slice MRIs. Based on these results, SRS would be a safe modality for preserving CN function in CS tumors. Aside from CN deficits, we also identified one carotid artery stenosis (0.8%). In previous reports on SRS for PA and CH, the incidence of radiation-induced ICA stenosis/occlusion range was 0.4–2.8% [44, 45]. Although ICA stenosis/occlusion is rare and rarely becomes symptomatic, long-term follow-up is needed.

This study has several limitations. First, it was a retrospective, single-institution study with potential selection bias. In addition, the clinical practice standards specific to the institution were used, thereby impairing the generalizability of the findings. Second, 38 tumors in this cohort were radiographically diagnosed, therefore the certainty of the diagnoses could be less reliable than those with histological confirmation. Finally, a larger sample size for each tumor type would be desirable for future studies to confirm our findings.

Conclusion

We confirmed that SRS achieved excellent treatment efficacy for benign skull base tumors invading the CS. It could achieve long-term tumor control and enable sufficient preservation of CN function.

Declarations

- **Funding:** This work was supported by JSPS KAKENHI (grant number 19K24042 to Yuki Shinya).
- **Conflicts of interest:** The authors have no conflicts of interest to declare that are relevant to the content of this article.
- **Ethics approval:** The study was approved by the Institutional Review Board of our institution (#2231) and performed in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.
- **Informed consent:** All patients provided written informed consent for study participation.
- **Data availability:** The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.
- **Author contributions:** Conceptualization: Motoyuki Umekawa, Yuki Shinya; Methodology: Motoyuki Umekawa, Yuki Shinya; Formal analysis and investigation: Motoyuki Umekawa, Yuki Shinya; Writing - original draft preparation: Motoyuki Umekawa; Writing - review and editing: Yuki Shinya, Hirotaka Hasegawa, Masahiro Shin, Mariko Kawashima, Atsuto Katano, and Nobuhito Saito.; Funding acquisition: Yuki Shinya; Resources: Yuki Shinya, Hirotaka Hasegawa, Shin Masahiro, Mariko Kawashima, Atsuto Katano; Supervision: Masahiro Shin and Nobuhito Saito.

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Figures

Figure 1

Kaplan–Meier curves for (A) progression-free survival rates for the entire cohort, (B) progression-free survival rates comparing meningiomas, trigeminal schwannomas (TS), pituitary adenomas (PA), and cavernous hemangiomas (CH), (C) progression-free survival rates comparing SRS alone and SRS with prior surgery, and (D) progression-free survival rates in meningioma comparing SRS alone and SRS with prior surgery.

Figure 2

Kaplan–Meier curves for cranial nerve function improvement rates after radiosurgery in all tumors (A) and improvement rates comparing meningiomas, trigeminal schwannomas (TS), pituitary adenomas (PA), and cavernous hemangiomas (CH) (B). Kaplan–Meier curves of cranial nerve function deterioration rates after radiosurgery in all tumors (C) and deterioration rates comparing meningiomas, trigeminal schwannomas (TS), pituitary adenomas (PA), and cavernous hemangiomas (CH) (D).

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